

We claim:

1. A method of treating a subject suffering from a lysosomal storage disorder other than Fabry Disease caused by a deficiency of a specific protein comprising:

5

- (a) producing said protein or an active fragment thereof in an insect cell culture, and
- (b) administering a therapeutically effective amount of said protein to said subject.

10

2. The method of claim 1 wherein said lysosomal storage disorder is selected from the group consisting of Pompe Disease, GM1 gangliosidosis, Tay-Sachs disease, GM2 gangliosialidosis: AB Variant, Sandhoff Disease, Gaucher Disease, Krabbe Disease, Niemann-Pick Types A-D, Farber Disease, Wolman Disease, Cholesterol Ester Storage Disease, Hurler Syndrome, Scheie Syndrome, Hurler-Scheie, Hunter Syndrome, Sanfilippo A-D, Morquio A-B, Maroteaux-Lamy, Sly Syndrome, Metachromatic Leukodystrophy, Multiple Sulfatase Deficiency, Sialidosis, I-Cell Disease, Pseudo-Hurler Polydystrophy, Mucopolipidosis IV,  $\alpha$ -Mannosidosis,  $\beta$ -Mannosidosis, Fucosidosis, Aspartylglucosaminuria, Galactosialidosis, Schindler Disease, Cystinosis, Salla Disease, Infantile Sialic Acid Storage Disorder, Batten Disease, Infantile Neuronal Ceroid Lipofuscinosis, and Prosaposin.

20

3. The method of claim 1 wherein said protein is selected from the group consisting of acid  $\alpha$ -1,4 glucosidase, acid  $\alpha$ -1,6 glucosidase,  $\beta$ -galactosidase,  $\beta$ -hexosaminidase A, GM<sub>2</sub> Activator Protein,  $\beta$ -hexosaminidase A,  $\beta$ -hexosaminidase B, glucocerebrosidase,  $\beta$ -glucosidase, galactosylcerebrosidase, acid sphingomyelinase, acid ceramidase, acid lipase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -N-acetylglucosaminidase, acetyl-CoA-glucosaminide acetyltransferase, N-acetylglucosamine-6-sulfatase, galactosamine-6-sulfatase, arylsulfatase B,  $\beta$ -glucuronidase, arylsulfatase A, arylsulfatase C,  $\alpha$ -Neuraminidase, UDP GlcNAc:lysosomal-enzyme N-acetylglucosamine-1-phosphotransferase, neuraminidase,  $\alpha$ -mannosidase,  $\beta$ -mannosidase,  $\alpha$ -L-fucosidase, N-aspartyl- $\beta$ -glucosaminidase, protective protein/cathepsin A (PPCA),  $\alpha$ -N-acetyl-

30

galactosaminidase, cystine transport protein, sialic acid transport protein, palmitoyl-protein thioesterase, and Saposins A-D.

4. The method of claim 1 wherein said protein is produced in an insect cell culture using a baculovirus expression system.

5. The method of claim 1 wherein said insect cell culture is derived from the species *Spodoptera frugiperda*.

6. The method of claim 5 wherein said insect cell culture is an Sf9 cell culture.

7. A method of treating a subject with a protein other than  $\alpha$ -galactosidase that is therapeutically active when present in a macrophage comprising:

- (a) producing said protein in an insect cell culture; and
- (b) administering a therapeutically effective amount of said protein to said subject.

8. A pharmaceutical composition comprising a protein useful for treating a lysosomal storage disorder other than Fabry disease that is selectively imported into macrophages when administered to a subject and a pharmaceutically acceptable carrier, wherein said protein is produced in an insect cell culture.

9. The composition of claim 8 wherein said lysosomal storage disorder is selected from the group consisting of Pompe Disease, GM1 gangliosidosis, Tay-Sachs disease, GM2 gangliosialidosis: AB Variant, Sandhoff Disease, Gaucher Disease, Krabbe Disease, Niemann-Pick Types A-D, Farber Disease, Wolman Disease, Cholesterol Ester Storage Disease, Hurler Syndrome, Scheie Syndrome, Hurler-Scheie, Hunter Syndrome, Sanfilippo A-D, Morquio A-B, Maroteaux-Lamy, Sly Syndrome, Metachromatic Leukodystrophy, Multiple Sulfatase Deficiency, Sialidosis, I-Cell Disease, Pseudo-Hurler Polydystrophy, Mucopolipidosis IV,  $\alpha$ -Mannosidosis,  $\beta$ -Mannosidosis, Fucosidosis, Aspartylglucosaminuria, Galactosialidosis, Schindler

Disease, Cystinosis, Salla Disease, Infantile Sialic Acid Storage Disorder, Batten Disease, Infantile Neuronal Ceroid Lipofuscinosis, and Prosaposin.

10. The composition of claim 8 wherein said protein is selected from the group consisting of acid  $\alpha$ -1,4 glucosidase, acid  $\alpha$ -1,6 glucosidase,  $\beta$ -galactosidase,  $\beta$ -hexosaminidase A, GM<sub>2</sub> Activator Protein,  $\beta$ -hexosaminidase A,  $\beta$ -hexosaminidase B, glucocerebrosidase,  $\beta$ -glucosidase, galactosylcerebrosidase, acid sphingomyelinase, acid ceramidase, acid lipase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -N-acetylglucosaminidase, acetyl-CoA-glucosaminide acetyltransferase, N-acetylglucosamine-6-sulfatase, galactosamine-6-sulfatase, arylsulfatase B,  $\beta$ -glucuronidase, arylsulfatase A, arylsulfatase C,  $\alpha$ -Neuraminidase, UDP GlcNAc:lysosomal-enzyme N-acetylglucosamine-1-phosphotransferase, neuraminidase,  $\alpha$ -mannosidase,  $\beta$ -mannosidase,  $\alpha$ -L-fucosidase, N-aspartyl- $\beta$ -glucosaminidase, protective protein/cathepsin A (PPCA),  $\alpha$ -N-acetyl-galactosaminidase, cystine transport protein, sialic acid transport protein, palmitoyl-protein thioesterase, and Saposins A-D.

11. The composition of claim 8 wherein said insect cell culture comprises cells derived from the species selected from the group consisting of *Spodoptera frugiperda* and *Tricoplusia ni*.

12. The composition of claim 11 wherein said cells are *Spodoptera frugiperda* Sf9 cells.

13. The composition of claim 8 wherein said protein is produced in the cell culture using a baculovirus expression system.

14. A method for producing a protein associated with a lysosomal storage disorder other than  $\alpha$ -galactosidase, protective protein/cathepsin A (PPCA), cathepsin B, cathepsin S,  $\beta$ -galactosidase,  $\beta$ -hexosaminidase B, neuraminidase, lysosomal acid lipase, prorenin, glucocerebrosidase and lysosomal acid alpha-glucosidase in a form that is

selectively imported into macrophages when administered to a subject comprising producing said protein in an insect cell culture.

15. The method of claim 14 wherein said lysosomal storage disorder is selected from the group consisting of GM2 gangliosialidosis: AB Variant, Sandhoff Disease, Krabbe Disease, Niemann-Pick Types A-D, Farber Disease, Hurler Syndrome, Scheie Syndrome, Hurler-Scheie, Hunter Syndrome, Sanfilippo A-D, Morquio A, Maroteaux-Lamy, Sly Syndrome, Metachromatic Leukodystrophy, Multiple Sulfatase Deficiency, I-Cell Disease, Pseudo-Hurler Polydystrophy, Mucopolipidosis IV,  $\alpha$ -Mannosidosis,  $\beta$ -Mannosidosis, Fucosidosis, Aspartylglucosaminuria, Schindler Disease, Cystinosis, Salla Disease, Infantile Sialic Acid Storage Disorder, Batten Disease, Infantile Neuronal Ceroid Lipofuscinosis, and Prosaposin.

16. The method of claim 14 wherein said protein is selected from the group consisting of GM<sub>2</sub> Activator Protein,  $\beta$ -hexosaminidase A,  $\beta$ -hexosaminidase B, galactosylcerebrosidase, acid sphingomyelinase, acid ceramidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -N-acetylglucosaminidase, acetyl-CoA-glucosaminide acetyltransferase, N-acetylglucosamine-6-sulfatase, galactosamine-6-sulfatase, arylsulfatase B,  $\beta$ -glucuronidase, arylsulfatase A, arylsulfatase C, UDP GlcNAc:lysosomal-enzyme N-acetylglucosamine-1-phosphotransferase, neuraminidase,  $\alpha$ -mannosidase,  $\beta$ -mannosidase,  $\alpha$ -L-fucosidase, N-aspartyl- $\beta$ -glucosaminidase,  $\alpha$ -N-acetyl-galactosaminidase, cystine transport protein, sialic acid transport protein, palmitoyl-protein thioesterase, and Saposins A-D,

17. A protein-conjugate complex that is selectively imported into macrophages when administered to a subject wherein the protein component of said protein-conjugate complex is produced in an insect cell culture.

18. A method for increasing the ability of a cell to uptake a protein produced in an insect cell culture comprising causing said cell to express a mannose receptor on its membrane.

19. A system for targeting a protein to a desired cell comprising:

- (a) causing said cell to express a mannose receptor on its membrane;
- 5 (b) producing said protein in an insect cell culture; and
- (c) contacting said protein with said cell.

20. In a method for purifying a protein produced in an insect cell culture using a  
Concanavalin A-Sepharose column, an improvement comprising the use of a buffer  
10 containing methyl- $\alpha$ -D-manno-pyranoside to elute said protein from said  
Concanavalin A-Sepharose column.